Chapter 10
Acute Decompensated Heart Failure: Treatment Guidelines

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Treatment of ADHF: Review of ACCF/AHA, ESC and HFSA Guidelines

Comprehensive guidelines for the management of ADHF have been published including: the American College of Cardiology Foundation/American Heart Association (ACCF/AHA) Guidelines for the Management of Heart Failure [1], the Heart Failure Society of America (HFSA) Comprehensive Practice Guidelines [2, 3], and the European Society of Cardiology (ESC) Task Force Guidelines [4].

There are three phases in the evaluation and management of patients who present with ADHF including [2, 5, 6]:

1. Initial assessment, monitoring, treatment and disposition. This phase generally occurs in the emergency department (ED).
2. Ongoing assessment and treatment. This phase generally occurs in a critical care or telemetry unit. Goals of treatment are to relieve congestion, initiate and/or optimize guideline determined medical therapy (GDMT), and further evaluate and address reversible factors that cause or worsen heart failure.
3. Discharge planning and post-discharge follow up.

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Initial Assessment and Treatment in the Emergency Department

A number of important issues need to be addressed as part of the initial assessment of a patient who presents to the ED with the primary symptom of dyspnea. These issues need to be addressed concurrently and often, treatment needs to be initiated in parallel with the ongoing diagnostic evaluation:

1. Is the patient's condition immediately life-threatening because of hypoxia, respiratory failure, hypotension, systemic hypoperfusion, bradyarrhythmia and/or tachyarrhythmia? Does the patient need mechanical ventilation, intravenous vasoactive medications, an intra-aortic balloon pump or other mechanical circulatory support, ventricular pacing, or cardioversion?
2. Is the patient having an acute coronary syndrome precipitating heart failure? Does the patient need to go emergently to the cardiac catheterization laboratory for percutaneous coronary intervention (PCI)?
3. Does the patient have heart failure? Is there an alternative cause of symptoms?
4. Are there precipitating factors that have caused or contributed to acute heart failure decompensation?
5. Relieve symptoms rapidly while avoiding harm. Improvement in symptoms generally requires relief of pulmonary congestion and improvement in elevated blood pressure without causing hypotension, arrhythmia, electrolyte abnormality, renal dysfunction, myocardial injury or respiratory compromise.
6. Does the patient need to be admitted to the hospital (CCU or telemetry floor), observed further in the ED, admitted to an observation unit, or discharged to home?

Initial Triage

Patients who present with acute dyspnea need to be assessed for the presence of pulmonary or hemodynamic instability that may require emergent intervention. Patients who present with tachypnea, hypoxia not readily corrected with nasal oxygen, respiratory distress or mental status changes may need emergent intervention with noninvasive ventilation or endotracheal intubation. While arterial blood gas determination is not routine in the assessment of most patients presenting with ADHF, it should be obtained in the patient with impending respiratory failure or severe lung disease. Endotracheal intubation and mechanical ventilation should be considered in patients with respiratory acidosis.

In EHFS II, ACS was the precipitating factor in 42 % of patients who presented with new onset heart failure and 23 % of patients who had preexisting heart failure. Patients with ACS generally present with precordial chest pain [7]. A 12-lead ECG is a critical part of the early evaluation of patients with suspected ADHF as the presence of ST segment elevation (or new LBBB) in the setting of an elevated

troponin is an indication for emergent coronary intervention as outlined in recent consensus documents [1, 8]. Patients may have ST segment depression and /or T wave inversion that, combined with clinical symptoms suggestive of ischemia and elevated troponin, are indicative of ACS [9]. ST-T wave changes alone may not be diagnostic of coronary ischemia or infarction and may be observed in other conditions including acute pericarditis, early repolarization patterns, LBBB, LV hypertrophy, and Brugada syndrome [10]. The ECG is helpful in identifying underlying heart rhythm abnormalities which may need urgent treatment (e.g. atrial fibrillation with rapid ventricular response, ventricular tachycardia, heart block).

Abnormal ECG findings are not helpful in discriminating HF from other causes of dyspnea (sensitivity 0.5, specificity 0.78 and positive likelihood ratio of 2.2). Atrial fibrillation, however, has a specificity of 0.93 and a positive likelihood ratio of 3.8 [11]. However, it is unlikely for patients with systolic dysfunction to have an entirely normal ECG. In a screening study of 534 patients with suspected heart failure, 96 patients had systolic dysfunction on echocardiography. Of these, 90 had major electrocardiographic abnormalities (atrial fibrillation, previous myocardial infarction, left ventricular hypertrophy, bundle branch block, or left axis deviation); none had a normal electrocardiogram. Of 438 patients with normal left ventricular systolic function, 169 had major electrocardiographic abnormalities [12].

Patients with STEMI, acute decompensation of chronic heart failure or acute heart failure due to myocardial inflammation may present with hypotension, evidence of compromised end-organ perfusion and pulmonary congestion. These patients commonly have sinus tachycardia, hypotension, a narrow pulse pressure, and evidence of pulmonary and systemic venous congestion. This subset of critically ill patients may need inotropic and/or vasopressor support, pulmonary artery catheterization to guide therapy and mechanical support with an IABP, Impella, TandemHeart, or extracorporeal life support (ECLS) [8].

Determination of either BNP or NT-proBNP is recommended in patients with dyspnea and signs and symptoms consistent with heart failure. The use of either biomarker is most helpful when there is an intermediate pretest probability of heart failure and the values are either very low or very high. Age, gender, renal function and obesity may affect natriuretic peptide levels. Levels should not be interpreted in isolation but rather, in the context of the broader clinical evaluation.

A BNP level < 100 pg/mL has a sensitivity, specificity, negative predictive and positive predictive value of 90 %, 76 %, 79 %, and 89 %, respectively [13]. BNP levels tend to increase with age. In patients less than 70 years of age, a BNP level >400 pg/mL has a sensitivity of 60 %, specificity of 95 %, positive predictive value of 86 %, negative predictive value of 81 % and diagnostic accuracy of 82 %. In patients ≥ 70 years of age, a BNP level >400 pg/mL has a sensitivity of 65 %, specificity of 83 %, positive predictive value of 86 %, negative predictive value of 60 % and diagnostic accuracy of 72 % [14]. Approximately 75 % of patients who present with acute dyspnea will have either low (<100 pg/mL) or high (>400–500 pg/mL) BNP levels. In general, in patients who present to the ED with dyspnea, if the BNP is <100 pg/ml, heart failure is unlikely to be the cause of dyspnea. If the BNP is >500 pg/ml, HF is likely with a positive predictive value of 90 %.

With BNP levels between 100–500 pg/ml, alternative causes of increased BNP need to be considered including stable chronic LV dysfunction, RV failure due to cor pulmonale, acute pulmonary embolism or renal insufficiency. Patients may present with HF and normal BNP levels in the following settings: flash pulmonary edema within 1–2 h of onset, HF upstream from the left ventricle, (e.g., acute papillary muscle rupture with acute mitral regurgitation), and obesity. In patients with a body mass index >35 kg/m^2, a BNP cutoff of 60 pg/mL has been recommended to rule out and 200 pg/mL to rule in HF as the cause of acute dyspnea. In general, BNP is elevated in the setting of chronic renal insufficiency. It may be reasonable to recalibrate the BNP cutoff to 200–225 pg/mL in patients with an estimated glomerular filtration rate of <60 mL/min to rule out heart failure. BNP levels are lower in obese people with and without heart failure. There seems to be a linear decrease in BNP level with increasing BMI [15, 16]. In general, in patients with chronic heart failure, changes of >50 % from baseline represent worsening heart failure. However, significant variation in levels can occur in the same patient and individual differences in NP do not necessarily represent an acute clinical event. There is a substantial grey zone in interpreting the results [17].

An NT-proBNP <300 pg/ml has a 99 % negative predictive value to exclude heart failure in patients who present with dyspnea. This is independent of age and BMI [18]. An NT-proBNP >900 pg/mL has a sensitivity of 90 %, specificity of 85 % and positive predictive value of 76 % to predict heart failure as the cause of dyspnea [19]. Age stratification of NT-proBNP using cut points of 450, 900, and 1800 pg/ml for age groups of <50, 50–75, and >75 years, respectively reduces false-negative findings in younger patients, reduces false-positive findings in older patients, and improves the overall positive predictive value without a change in overall sensitivity or specificity. These cut-points have a 90 % sensitivity and 84 % specificity for acute HF [20, 21] and are predictive of acute heart failure across a wide range of BMIs [22].

Initial Treatment

The HFSA and ESC guidelines recommend that oxygen should be administered by nasal cannula or face mask in patients with hypoxia but is not recommended in the absence of hypoxia. The HFSA and ESC guidelines recommend the use of non-invasive positive pressure ventilation for patients with severe dyspnea and clinical evidence of pulmonary edema [2, 4]. The ESC guidelines specifically recommend non-invasive ventilation in patients with dyspnea, evidence of pulmonary edema and a respiratory rate of >20 breaths/minute.

The ESC Guidelines recommend that IV morphine sulfate (MS) should be considered, especially in anxious, restless or distressed patients to relieve these symptoms and improve breathlessness. However, the HFSA guidelines recommend that

if used at all, MS should be used with caution given recent data demonstrating an association between MS use and adverse outcomes.

Treatment with an intravenous loop diuretic is consistently recommended in the ACCF/AHA, ESC and HFSA guidelines as first line treatment in the initial management of patients with ADHF and that diuretic therapy should be initiated in the ED without delay [1, 2, 4]. Although there are no randomized placebo-controlled clinical trials to establish the safety and efficacy of diuretics in ADHF, extensive observational experience has shown that diuretics relieve congestion and improve symptoms. The impact of diuretic therapy on mortality has not been adequately studied.

The HFSA Guidelines do not make specific recommendations about initial diuretic dose. The ACCF/AHA Guidelines recommend that in patients already receiving a loop diuretic, the initial diuretic dose should equal or exceed their chronic oral daily dose and be given either as intermittent intravenous boluses or continuous infusion [1]. The ESC Guidelines recommend that an initial dose of furosemide 20–40 mg IV (or 0.5–1.0 mg bumetanide IV or 10–20 mg of torsemide IV) be given on admission. In patients with evidence of volume overload, a higher dose of parenteral diuretic may be considered based on renal function and history of chronic oral diuretic use. Continuous infusion may also be considered after an initial starting bolus dose. ESC recommends that the total furosemide dose should remain <100 mg in the first 6 h and 240 mg during the first 24 h [5].

Indications for Hospitalization

Recommendations for hospitalization from the HFSA Guidelines are summarized in Table 10.1 [2]. A recently published consensus document from the Society for Academic Emergency Medicine/Heart Failure Society of America Acute Heart Failure Working Group has suggested that ED patients with ADHF can be divided into three groups based on risk profile, presence of co-morbidities, initial response to therapy in the ED and barriers to self-care [23]. Patients at high risk for mortality or serious adverse events (those with low blood pressure, hypoxia, renal insufficiency or myocardial ischemia/infarction) should be admitted to the CCU.

Identifying Precipitating Causes of Acute HF Decompensation

An essential task in the evaluation of a patient who presents with acute decompensated heart failure is to identify new or chronic issues/conditions that may cause, precipitate or contribute to heart failure decompensation. This should be done early in the evaluation so that appropriate therapies can be initiated, symptoms can be

Table 10.1 Recommendations for hospitalizing patients presenting with ADHF

Recommendation	Clinical circumstance
Hospitalization recommended	Evidence of severely decompensated HF, including: Hypotension Worsening renal function Altered mentation
	Dyspnea at rest
	Typically reflected by resting tachypnea; less commonly reflected by oxygen saturation <90 %
	Hemodynamically significant arrhythmia; including new onset of rapid atrial fibrillation
	Acute coronary syndromes
Hospitalization should be considered	Worsened congestion
	Even without dyspnea
	Signs and symptoms of pulmonary or systemic congestion; even in the absence of weight gain
	Major electrolyte disturbance
	Associated comorbid conditions:
	Pneumonia
	Pulmonary embolus
	Diabetic ketoacidosis
	Symptoms suggestive of transient ischemic accident or stroke
	Repeated ICD firings
	Previously undiagnosed HF with signs and symptoms of systemic or pulmonary congestion

Reprinted from Lindenfeld et al. [2]

alleviated more rapidly, reversible myocardial dysfunction can be treated and recurrent heart failure hospitalizations can be prevented. Table 10.2 summarizes conditions that can cause or contribute to the development of acute decompensated heart failure.

Co-morbid conditions are common and play a significant role in hospitalization for ADHF. In the OPTIMIZE-HF registry, one or more precipitating factors were identified in 61.3 % of patients admitted with ADHF. The most common precipitating factors included: pneumonia/respiratory process (15.3 %), ischemia/acute coronary syndrome (14.7 %), arrhythmia (13.5 %), and poorly controlled hypertension (10.7 %). Nonadherence to medications was identified in 8.9 % and nonadherence to diet was identified in 5.2 % [24].

Coronary Artery Disease

Coronary artery disease is present in approximately 50–70 % of patients with ADHF [7, 25–30]. Patients may present with ACS complicated by heart failure or ADHF with underlying CAD.

Table 10.2 Possible precipitating causes of heart failure decompensation

Coronary artery disease
Myocardial ischemia
ACS
Mechanical complications of AMI (VSD, MR)
Valvular disease
Mitral regurgitation: worsening chronic or acute
Progressive aortic stenosis
Worsening tricuspid insufficiency
Aortic insufficiency
Endocarditis
Aortic dissection
Progressive cardiac dysfunction
Progression of underlying cardiac dysfunction
Physical, emotional or environmental stress
Cardiac toxins – alcohol, cocaine, methamphetamines, chemotherapy
RV pacing
Persistent tachycardia
Frequent PVCs
Myocardial disease
Lymphocytic myocarditis
Giant cell myocarditis
Post-partum cardiomyopathy
Sarcoid
Uncontrolled high blood pressure
Dietary and medication adherence
Excessive salt and water intake
Medication nonadherence
Iatrogenic volume expansion
Arrhythmia
Atrial fibrillation
Atrial flutter
Other supraventricular arrhythmia
Recurrent ventricular tachycardia
Bradycardia-sinus node dysfunction, heart block, AF with slow ventricular response
Recent onset LBBB
Non-cardiac conditions
Systemic infection: sepsis, pneumonia, URI, UTI, viral infection (especially influenza)
Renal insufficiency
Thyroid disorders
Anemia
COPD/asthma
Sleep apnea
Pulmonary embolism

(continued)

Table 10.2 (continued)

AV shunts
Urinary outlet obstruction
Tamponade
Iron deficiency
CVA
Depression, dementia, and cognitive impairment
Recent addition of medications with negative inotropic effects:
Calcium channel blockers: especially the non-dihydropyridines verapamil and diltiazem
Class Ia, Ic and III antiarrhythmic medications:
Quinidine, procainamide, disopyramide, flecainide, sotalol, propafenone, dronedarone
β-adrenergic blocking agents
Non-cardiac medications that promote sodium retention:
Nonsteroidal anti-inflammatory drugs
COX-2 inhibitors
Corticosteroids
Thiazolidinediones
Pregabalin
Chemotherapy
Anthracyclines
Monoclonal antibodies – Trastuzumab and Bevacizumab
Taxanes – paclitaxel and docetaxel
Cyclophosphamide
Small tyrosine kinase inhibitors – Sunitinib, sorafenib, imatinib

ACS Complicated by Heart Failure

Approximately 10–20 % of patients with ACS have associated heart failure on presentation and another 10 % of ACS patients develop heart failure during hospitalization. Patients with ACS due to a STEMI typically have chest pain, diagnostic ECG changes and high levels of biomarkers consistent with substantial myocardial injury [29]. Patients with heart failure complicating an STEMI (either on presentation or developing later after hospitalization) have significantly increased in-hospital and post-discharge mortality compared to patients without heart failure [29–32]. Patients with ACS who develop heart failure after admission are at greater risk than patients with ACS who have heart failure on presentation [30, 32]. The severity of heart failure measured by the Killip classification is a powerful predictor of mortality in patients with heart failure complicating ACS. Patients with Killip class II or III are 4 times more likely to die during hospitalization compared with Killip class I patients while patients with Killip class IV (cardiogenic shock) are 10 times more likely [30, 32]. Patients with heart failure and unstable angina have also been found have a significant fourfold increase in mortality compared to similar patients without HF [31].

The Global Registry of Acute Coronary Events (GRACE) enrolled 16,166 patients with ACS. Patients who presented with HF complicating ACS had lower rates of catheterization and PCI and were less likely patients receive β-blockers and statins [31]. In the National Registry of Myocardial Infarction (NRMI), patients with HF complicating ACS were less likely to receive aspirin, heparin, intravenous nitroglycerine and β-blockers compared to patients with ACS without heart failure. In addition, patients with heart failure were less likely to undergo PCI or CABG compared with patients without heart failure on presentation (40 % vs 20 %) [32].

An analysis of the Can Rapid Risk Stratification of Unstable Angina Patients Suppress Outcomes with Early Implementation of the American College of Cardiology/American Heart Association (ACC/AHA) Guidelines (CRUSADE) initiative (2.8 % of patients had HF) demonstrated that patients with a non-STEMI with heart failure with preserved EF had a significantly higher mortality rate than patients without HF and preserved systolic function and a similar mortality to patients with no HF and systolic dysfunction. Patients with both HF and systolic dysfunction had the highest mortality (1.5 % vs 5.7 % vs 5.8 % vs 10.7 %). Cardiac catheterization and PCI rates were lower for patients without heart failure with systolic dysfunction and with HF with or without systolic dysfunction. Patients with HF received aspirin, clopidogrel, glycoprotein IIb/IIIa inhibitors, heparin, B-blockers and statins less frequently than patients with no HF and preserved systolic function [33].

There is broad consensus that patients with HF complicating ACS should undergo urgent coronary angiography and coronary intervention in the catheterization laboratory [1, 2, 9, 34, 35].

ADHF with Underlying CAD

It has been estimated that 50–70 % of patients with ADHF have concomitant coronary artery disease. Registry data suggest that CAD is associated with higher in-hospital and post-discharge mortality rates. In the OPTIMIZE – Registry, in-hospital mortality rates were 3.75 % vs 2.9 % and post-discharge 60–90 day mortality rates were 9.2 vs 6.9 % in patients with CAD vs no CAD [36].

In multicenter registries of patients admitted with ADHF, rates of diagnostic coronary angiography are relatively low overall: OPTIMIZE –HF 8.7 % [36]; ADHERE 10 % [25]; EHFS 16 % [27]; and EHFS II 36.5 % (EHFS II reported angiography within a year of hospitalization) [7]. In OPTIMIZE-HF, 18.6 % of patients presenting with de novo heart failure underwent coronary angiography [36]. Rates of coronary revascularization were relatively low: ADHERE 8.1 % PCI, 1.8 % CABG [25]; EHFS PCI 4 %, CABG 3 % [27]; EHFS II PCI 8.4 %, CABG 1.8 % [7]; OPTIMIZE-HF 1.3 % PCI, 1.0 % CABG [37].

In OPTIMIZE-HF, patients with CAD who did not undergo revascularization had a higher post-discharge mortality compared to patients without CAD (10.6 vs

6.9 %). Patients who did undergo revascularization during HF hospitalization had a similar post-discharge mortality compared to patients without CAD [36].

The data from the OPTIMIZE-HF registry was analyzed to determine if the performance of coronary angiography during the index HF hospitalization had an impact on care and post-discharge outcome [37]. 8.7 % of all patients underwent coronary angiography. 27.5 % of patients who underwent angiography also had in-hospital revascularization. Patients with CAD who underwent angiography were more likely to be treated with aspirin, statins, B-blockers, and angiotensin converting enzyme inhibitors at the time of discharge. In patients with CAD, the use of in-hospital coronary angiography was associated with a significantly lower mortality and rate of rehospitalization in the first 60–90 days after adjustment for multiple comorbidities (mortality HR 0.31; $p = 0.004$; death or rehospitalization HR 0.65; $p = 0.003$) when compared to patients with CAD who did not undergo coronary angiography. This data suggests that early coronary angiography and revascularization may be beneficial in patients admitted to the hospital with CAD and ADHF.

These results were registry based and may not account for unmeasured variables or selection biases. In the randomize Surgical Treatment for Ischemic Heart Failure (STICH) trial, there was no difference in death from any cause in patients with LVEF ≤ 35 % and coronary artery disease amenable to CABG randomized to medical therapy or medical therapy plus CABG on intention to treat analysis. However, when early crossovers were considered, "on-therapy" CABG was associated with a lower mortality at 5 years (25 % vs 42 %; HR 0.50; p=0.008). Myocardial viability or inducible myocardial ischemia did not identify patients with a differential survival benefit from CABG compared to medical therapy alone [38–40].

Practice guidelines provide recommendations on the use of coronary angiography in the evaluation of patients with chronic heart failure. However, they do not give specific recommendations about the timing of invasive evaluation of coronary anatomy and specifically do not provide recommendations about indications for coronary angiography in patients hospitalized for ADHF. Given the absence of definitive data concerning coronary angiography and revascularization in ADHF, decisions should be individualized based on patient preference, symptoms, clinical presentation, comorbidities, candidacy for revascularization and willingness to undergo revascularization [1, 2]. In general, coronary angiography is recommended for patients with heart failure and symptoms suggestive of angina to assess for the possibility of revascularization. Non-invasive imaging *or* coronary angiography is recommended for patients with new onset heart failure, no angina and unknown CAD status and patients with new or worsening heart failure without obvious cause, no angina and known CAD. Recommendations from the HFSA Guidelines for the evaluation for CAD in patients with ADHF are reviewed in Table 10.3 [2].

Uncontrolled Hypertension

Hypertension is an important precipitant of decompensated heart failure, especially among blacks, women and patients with HFpEF. In the OPTIMIZE-HF registry, poorly controlled hypertension was a precipitating factor in 10.7 % of patients [24]. In

Table 10.3 HFSA Guidelines for the evaluation for CAD in patients with ADHF

Ongoing assessment for risk factors for CAD is recommended in all patients with chronic HF regardless of LVEF. (Strength of Evidence = A)
It is recommended that the diagnostic approach for CAD be individualized based on patient preference and comorbidities, eligibility, symptoms suggestive of angina and willingness to undergo revascularization. (Strength of Evidence = C)
It is recommended that patients with HF and symptoms suggestive of angina undergo cardiac catheterization with coronary angiography to assess for potential revascularization. (Strength of Evidence = B)
It is recommended that, at the initial diagnosis of HF and any time symptoms worsen without obvious cause, patients with HF, no angina, and known CAD should undergo risk assessment that may include noninvasive stress imaging and/or coronary angiography to assess severity of coronary disease and the presence of ischemia. (Strength of Evidence = C)
It is recommended that patients with HF, no angina, and unknown CAD status who are at high risk for CAD should undergo noninvasive stress imaging and/or coronary angiography to assess severity of coronary disease and the presence of ischemia. (Strength of Evidence = C)
In patients with HF, no angina, and unknown CAD status who are at low risk for CAD noninvasive evaluation should be considered and coronary angiography may be considered. (Strength of Evidence = C)
Any of the following imaging tests should be considered to identify inducible ischemia or viable myocardium:
Exercise or pharmacologic stress myocardial perfusion imaging
Exercise or pharmacologic stress echocardiography
Cardiac magnetic resonance imaging (MRI)
Positron emission tomography scanning (PET) (Strength of Evidence = B)

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the ADHERE Registry, almost 50 % of patients admitted with decompensated heart failure has an initial blood pressure of >140/90 mmHg [25]. Medical non-adherence with antihypertensive medications may result in an abrupt increase in blood pressure and precipitate worsening heart failure or acute pulmonary edema [1, 41].

Arrhythmia

Arrhythmia was a precipitating factor of heart failure decompensation in 13.5 % of patients enrolled in the OPTIMIZE-HF registry [24]. Atrial fibrillation (AF) is present in approximately 30–40 % of patients hospitalized with ADHF [7, 27, 35, 42–45]. New onset or newly diagnosed AF has been reported to occur in approximately 20 % percent of patients admitted with ADHF [35, 44, 45]. AF is associated with the loss of coordinated atrial contraction. In patients with heart failure and especially in patients with HFpEF, this may be associated with significantly decreased left ventricular filling, increased PCWP and decreased cardiac output. In AF with rapid ventricular response, ventricular filling is further compromised and myocardial ischemia and/or pulmonary edema may be precipitated [46, 47].

Atrial flutter, other supraventricular tachyarrhythmias and ventricular tachycardia may also precipitate acute heart failure. Frequent premature ventricular contractions (PVCs) may be associated with a distinct cardiomyopathy (PVC-related

cardiomyopathy) or worsening heart failure and LV dysfunction in the setting of a preexisting cardiomyopathy. In general, a PVC burden of approximately 20–24 % of all QRS complexes on a 24 h Holter monitor identifies a patient with LV systolic dysfunction who may improve with PVC ablation [48–51].

Medication and Dietary Non-adherence

Excessive sodium and fluid intake may contribute to heart failure decompensation. In the OPTIMIZE-HF Registry, non-adherence to diet was identified as a precipitating factor in 5.2 % of patients hospitalized for ADHF. Non-adherence to medication was a precipitating factor in 8.9 % of patients [24]. Non-adherence with diet or HF medication has been reported to be an even more common precipitating factor in some single-center studies [52, 53]. Factors that have been associated with medical non-adherence include more advanced NYHA functional class, minority ethnicity, lower financial status, and lack of perceived social support. Patient perception of barriers to medication adherence may also be fundamental to poor adherence. Frequently reported barriers include: forgetting to take medication, cost, too many pills taken per day, too frequent medication schedule and the belief that skipping one dose of medication will not have an adverse impact on the patient's condition [54, 55].

Patients with heart failure commonly have excessive and bothersome thirst mediated by activation of central arterial volume receptors and increased levels of angiotensin II both of which stimulate thirst centers in the brain. This leads to excessive sodium and water intake [56–59]. This is a particularly difficult issue in patients with severe heart failure who are not able to be treated with an ACE inhibitor or ARB at reasonable or target dose. In addition, older patients commonly have chemosensory deficits that decrease salt detection and sensitivity and increase salt affinity and intake. Salt affinity may be modifiable toward normal after >2 months of sodium restriction [60]. Patients may also be unaware of the salt content of foods they are consuming or may feel that they do not need to limit sodium intake. A careful review of the patient's history of dietary intake of sodium and free water (including "hidden" sources of free water such as fruit) is an important part of the assessment of patients admitted with ADHF.

Pneumonia or Other Pulmonary Processes

Pneumonia and other acute respiratory processes were the most common precipitating factor (15.3 %) identified in patients hospitalized for ADHF in the OPTIMIZE-HF registry [24]. Pulmonary infections may alter pulmonary function, cause hypoxia, and increase metabolic demands and are poorly tolerated by patients with heart failure. Pulmonary congestion in a patient with chronic obstructive pulmonary disease can compromise already marginal pulmonary function. Patients with heart failure are hypercoagulable and pulmonary embolus

may be a cause of HF decompensation [61–64]. Sleep disordered breathing is very common in patients with heart failure. It may worsen heart failure by causing hypoxia, increasing sympathetic nervous system activation and causing or worsening systemic hypertension. Sleep disordered breathing has also been associated with left ventricular remodeling, endothelial dysfunction with progression of coronary artery disease, left ventricular hypertrophy and atrial fibrillation [65–67].

Infection

Systemic bacterial or viral infection (pneumonia, urinary tract infection, influenza) are common precipitants of worsening heart failure. Infections increase metabolic demands. In addition, sepsis can cause reversible myocardial dysfunction likely mediated by release of pro-inflammatory cytokines [68, 69].

Thyroid Disease

Hypothyroidism and hyperthyroidism can cause or worsen heart failure. All patients seen for ADHF should have thyroid function studies obtained on admission. Approximately 20 % of patients admitted with ADHF are treated for thyroid disease and should have their therapy reevaluated during hospitalization [70, 71]. Amiodarone-induced hyperthyroidism (AIT) can cause severe worsening of heart failure with or without new or worsening arrhythmias and can be difficult to treat. The clinical presentation of AIT is variable and is often similar to other forms of thyrotoxicosis. However, AIT often occurs in elderly patients and may be "apathetic" with atypical symptoms such as reduced appetite and depression and absence of hyperactivity, tremor, nervousness and heat intolerance [72].

Medications

A number of non-cardiac medications can precipitate worsening heart failure. Nonsteroidal anti-inflammatory drugs and COX-2 inhibitors inhibit the physiologic production of vasodilatory and natriuretic prostanoids in the kidney and promote sodium and water retention, worsen renal function, inhibit the effect of ACE inhibitors, contribute to diuretic resistance and are associated with a significantly increased risk of hospitalization for heart failure [73].

The thiazolidinediones (TZD), (pioglitazone and rosiglitazone) used to treat diabetes, have been associated with the development of lower extremity edema and new or worsening heart failure [74]. These side effects are primarily due to fluid retention caused by TZD stimulation of the peroxisome proliferator-activated receptor-gamma (PPARγ). PPARγ-mediated activation of the collecting duct epithelium's sodium channel (ENaC) and stimulation of sodium transporters

in the proximal tubule contribute to salt and water retention [75, 76]. In addition, TZDs reduce systemic vascular resistance and may cause fluid extravasation by exposing the capillaries of the lower extremities to higher perfusion pressures. TZDs also increase the concentration of vascular endothelial growth factor which is a potent inducer of vascular permeability which may predispose patients to edema [77].

Insulin can also cause sodium retention mediated by stimulation of a broad range of sodium transporters in the proximal tubule, loop of Henle and distal tubule [74]. Pregabalin, which is frequently used to treat diabetic peripheral neuropathic pain, has also been reported to precipitate heart failure decompensation [78].

Cardiotoxicity is a common complication of many conventional and targeted biological anti-cancer medications [79–83]. Cocaine, excessive alcohol intake, and methamphetamine are associated with worsening heart failure [84–89].

A number of cardiac medications have negative inotropic properties and can worsen heart failure. Recent initiation or uptitration of β-blockers has been associated with worsening heart failure, especially in patients with severe ventricular dysfunction and those recently treated with inotropic agents. Calcium channel blockers (CCBs), especially the non-dihydropyridine CCBs, have been associated with worsening heart failure. A large number of antiarrhythmic agents may also precipitate worsening heart failure including quinidine, procainamide, disopyramide, flecainide, sotalol, propanone, and dronedarone.

Right Ventricular (RV) Pacing

Right ventricular pacing can lead to abnormal electrical and mechanical activation patterns (referred to as ventricular "dyssynchrony") which lead to adverse effects on left ventricular performance and hemodynamics, subsequent adverse effects on cardiac structure and function, and clinical heart failure.

Patients with a single lead pacemaker or ICD may develop gradually progressive sinus bradycardia in response to beta blocker or amiodarone therapy and present with worsening heart failure in the setting of recent onset ventricular pacing. A similar scenario may be seen in patients who develop atrial fibrillation with a slow ventricular response in the setting of beta blockade or amiodarone therapy. These patients may improve by pacemaker reprogramming that minimizes RV pacing or an upgrade to a device that provides biventricular pacing [90, 91].

Renal Dysfunction

Renal dysfunction is common in patients with ADHF. In the ADHERE registry, chronic renal insufficiency was reported in 30 % of patients and 21 % had a creatinine >2.0 mg/dL [25]. In OPTIMIZE-HF, the mean creatinine was 1.8 mg/dL [92].

Elevated BUN and creatinine may be manifestations of renal hypoperfusion in the setting of low cardiac output, high filling pressures and/or neurohormonal activation. In HF, renal cortical blood flow is especially decreased and tubulointerstitial damage may develop due to decreased local renal perfusion and increased venous congestion. Albuminuria can occur in heart failure and is a manifestation of both a loss of glomerular integrity and tubular damage. A high albumin load may also contribute to tubular damage [93]. In addition, patients with heart failure commonly have risk factors for both cardiac and renal disease including diabetes and hypertension that may contribute to renal insufficiency independent of hemodynamic derangements from heart failure. A gradual or acute reduction in renal function will decrease renal clearance of sodium and water, worsen diuretic resistance, contribute to inadequate blood pressure control, contribute to hyperkalemia, and worsen anemia all of which will contribute to worsening HF.

Benign prostatic hypertrophy is common in men over the age of 50 years and may contribute to urinary obstruction, impaired renal function and worsening heart failure in men with ADHF. The prevalence of histologically diagnosed prostatic hyperplasia increases from 40 to 50 percent in men age 51 to 60 years, to over 80 percent in men older than age 80 years [94]. A population based study from Olmstead County, Minnesota found that moderate to severe lower urinary tract obstructive symptoms were present in 13 % of men 40–49 years and 28 % of those older than 70 years [95]. An evaluation for urinary obstruction can easily performed using bladder scanning. We have found that routine bladder scanning of men hospitalized with ADHF who have an elevated creatinine or diuretic resistance is helpful in identifying lower urinary tract obstruction. Relief of urinary obstruction with placement of a urinary catheter commonly results in improvements in renal function, diuretic resistance, pulmonary and systemic venous congestion and heart failure symptoms..

Ongoing Assessment and Treatment

The goals of treatment for patients admitted with ADHF from the HFSA guidelines are summarized in Table 10.4 [2].

Most patients have a significant improvement within 1–6 h after diuretic administration [96]. However, when diuresis is inadequate to relieve symptoms, the ACCF/AHA, HFSA, and ESC guidelines recommend giving a higher dose of diuretic or adding a second thiazide or thiazide-like diuretic (hydrochlorothiazide, chlorothiazide or metolazone). The HFSA and ESC guidelines also recommend considering use of a continuous infusion of a loop diuretic. The ACCF/AHA guidelines note that low-dose dopamine added to loop diuretic therapy may be considered to improve diuresis and preserve renal function.

The ACCF/AHA, HFSA, and ESC guidelines suggest that veno-venous ultrafiltration may be considered in volume overloaded patients to treat congestive symptoms and relieve volume overload. The ACCF/AHA guidelines suggest that UF may

Table 10.4 HFSA treatment goals for patients admitted for ADHF

HFSA treatment goals for patients admitted for ADHF [2]
Improve symptoms, especially congestion and low-output symptoms Restore normal oxygenation
Optimize volume status
Identify etiology
Identify and address precipitating factors
Optimize chronic oral therapy
Minimize side effects
Identify patients who might benefit from revascularization
Identify patients who might benefit from device therapy
Identify risk of thromboembolism and need for anticoagulant therapy
Educate patients concerning medications and self-management of HF
Consider and, where possible, initiate a disease management program

Reprinted from Lindenfeld et al. [2]
HFSA Heart Failure Society of America

be appropriate "for patients with refractory congestion not responding to medical therapy". The HFSA guidelines state that UF "may be considered in lieu of diuretics".

The ACCF/ACC, HFSA, and ESC guidelines emphasize the importance of careful monitoring of vital signs, signs and symptoms of congestion, urine output, electrolytes and renal function after initiation of diuretic therapy. Excessive diuresis may result in hypotension and a reduction in cardiac output. During loop diuretic-induced natriuresis, intravascular volume is generally maintained by vascular "refilling' or re-equilibration as interstitial fluid moves from the interstitial space to the intravascular space. The rate of refilling varies among patients. During brisk diuresis, it is possible for the rate of diuresis to exceed the rate of refilling. This may result in low intravascular volume, inadequate cardiac filling, and hypotension despite persistent volume overload. Patients with HPpEF are at greater risk of diuretic-induced hypotension – these patients tend to be less volume overloaded and have a steep diastolic filling curve so that moderate reductions in intravascular volume may result in significant reductions in cardiac filling and cardiac output. Patients with infiltrative or restrictive cardiomyopathy may have diuretic induced hypotension in the setting of continued volume overload as elevated ventricular filling pressures are needed to maintain normal cardiac output [2, 97]. Diuresis that results in a decrease in ventricular filling pressures makes patients more sensitive to the hypotensive effects of other vasodilators used in the routine treatment of heart failure.

The ACCF/AHA and HFSA guidelines recommend that in the absence of symptomatic hypotension, intravenous nitroglycerine, nitroprusside or nesiritide may be considered as an addition to diuretic therapy for relief of dyspnea in patients with ADHF. Blood pressure should be monitored frequently and the vasodilator should be stopped or dose decreased if symptomatic hypotension occurs. The ESC Guidelines recommend NTG or nitroprusside in patients with pulmonary

congestion/edema provided SBP >110 mmHg to reduce pulmonary capillary wedge pressure. Caution is advised when using nitroprusside in patients with acute myocardial infarction.

The ACCF/AHA and HFSA guidelines suggest that the use of the intravenous inotropes dobutamine, milrinone, and dopamine (ACCF/AHA only) be limited to patients with LV dilation, LV systolic dysfunction and evidence of low cardiac output or end-organ dysfunction. Commonly, these patients will have low blood pressure and evidence of hypoperfusion manifest by cold clammy skin, cool distal extremities, decreased urine output and altered mentation. These agents may also be appropriate in patients who have evidence of elevated filling pressures and an inadequate response to diuretics and parenteral vasodilators or who have worsening renal function in response to diuretic therapy [2, 98]. The guidelines emphasize that there is no evidence to support the routine use of inotropic therapy in patients with acute decompensated heart failure. Patients treated with an inotrope should have frequent blood pressure monitoring and continuous cardiac rhythm monitoring as treatment with these agents has been associated with hypotension and an increased risk of atrial and ventricular arrhythmias. In the ESC guidelines, inotropic agents are not recommended unless the patient is hypotensive (systolic blood pressure of <85 mmHg) and has evidence of hypoperfusion.

The ACCF/AHA guidelines recommend that guideline determined medical therapy (GDMT) including ACEI or ARB, β-blocker and MRA be continued in patients with HFrEF hospitalized with ADHF in the absence of hemodynamic instability, worsening renal function or hypokalemia. In addition, the ACCF/AHA guidelines recommend that medications on admission be reassessed during the ADHF hospitalization and that GDMT be initiated in patients who have HFrEF who are not receiving appropriate GDMT. The HFSA guidelines recommend that "near optimal" pharmacologic therapy, including ACEI and β-blocker, be achieved during the heart failure hospitalization. The ESC guidelines recommend that ACEI or ARB, β-blocker, and MRA be initiated and up-titrated as appropriate in patients with HFrEF and that digoxin may provide symptom benefit and reduce the risk of HF hospitalization in patients with severe systolic HF.

The HFSA guidelines recommend fluid restriction of <2 L/day in patients with ADHF with moderate hyponatremia (serum sodium <130 mEq/L). Stricter fluid restriction may be considered in patients with more severe hyponatremia (serum sodium <125 mEq/L). The ACCF/AHA guidelines recommend fluid restriction and optimization of medications that modulate the RAAS and decrease thirst in patients hospitalized for ADHF who have hyponatremia. These guidelines also recommend consideration of a vasopressin antagonist in patients hospitalized with ADHF who have persistent severe hyponatremia and volume overload (hypervolemic hyponatremia) who are at risk for or are having cognitive symptoms despite water restriction and optimization of GDMT.

The ACCF/AHA and ECS guidelines do not recommend the routine use of invasive hemodynamic monitoring with pulmonary artery catheterization in patients hospitalized for ADHF. PA catheterization should be considered in a patient: who is refractory to pharmacologic therapy; who has persistent clinically significant

hypotension; who has significantly worsening renal function in response to therapy; or whose volume status and cardiac filling pressures are uncertain.

The ACCF/AHA, ECS and HFSA guidelines all recommend that patients hospitalized with ADHF who are not already anticoagulated receive venous thromboembolism (VTE) prophylaxis with an anticoagulant medication provided there are no contraindications to anticoagulation and in whom the risk-benefit ratio is favorable (ACCF/AHA). The HFSA guidelines recommend VTE prophylaxis with a mechanical device (intermittent pneumatic compression devices or graded compression stockings) in patients hospitalized with ADHF who have a contraindication to anticoagulation.

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